

SEQUENCE LISTING

*1100 Nicolaides, Nicholas C
Grasso, Luigi
Sass, Philip M

*1200 METHODS FOR GENERATING GENETICALLY ALTERED
ANTIBODY-PRODUCING CELL LINES WITH IMPROVED ANTIBODY
CHARACTERISTICS

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*1400 00/000,000

*1410 0000-11-07

*1600 16

*1700 PatentIn Ver. 2.1

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*2120 DNA

*2130 Artificial Sequence

*2200

*2210 Description of Artificial Sequence:oligonucleotide
primer

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*2210 Description of Artificial Sequence:oligonucleotide
primer

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primer

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<211> 859

<212> FRT

<213> Mus musculus

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Ala Gly Ala Thr Thr Ile Asp Leu Arg Leu Lys Asp Tyr Gly Val Asp
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Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe
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Glu Gly Leu Ala Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala
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Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser

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Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Gly Ser
115 120 125

Ala Ser Val Gly Thr Arg Leu Val Phe Asp His Asn Gly Lys Ile Thr
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Gln Lys Thr Pro Tyr Pro Arg Pro Lys Gly Thr Thr Val Ser Val Gln
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Ile Lys Lys Glu Tyr Ser Lys Met Val Gln Val Leu Gln Ala Tyr Cys
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Ile Ile Ser Ala Gly Val Arg Val Ser Cys Thr Asn Gln Leu Gly Gln
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Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile
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Pro Phe Val Gln Leu Pro Pro Ser Asp Ala Val Cys Glu Glu Tyr Gly
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Leu Ser Thr Ser Gly Arg His Lys Thr Phe Ser Thr Phe Arg Ala Ser
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Phe His Ser Ala Arg Thr Ala Pro Gly Gly Val Gln Gln Thr Gly Ser
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Phe Ser Ser Ser Ile Arg Gly Pro Val Thr Gln Gln Arg Ser Leu Ser
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Leu Ser Met Arg Phe Tyr His Met Tyr Asn Arg His Gln Tyr Pro Phe
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Val Val Leu Asn Val Ser Val Asp Ser Glu Cys Val Asp Ile Asn Val
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Ala Val Leu Lys Thr Ser Leu Ile Gly Met Phe Asp Ser Asp Ala Asn

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365

Lys Leu Asn Val Asn Gln Gln Pro Leu Leu Asp Val Glu Gly Asn Leu
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Val Lys Leu His Thr Ala Gln Leu Glu Lys Pro Val Pro Gly Lys Gln
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Asp Asn Ser Pro Ser Leu Lys Ser Thr Ala Asp Glu Lys Arg Val Ala
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Ser Ile Ser Arg Leu Arg Glu Ala Phe Ser Leu His Pro Thr Lys Glu
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Ser Glu Lys Arg Gly Val Leu Ser Ser Tyr Pro Ser Asp Val Ile Ser
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Val Ala Ser Ser Phe Ser Ser Asp Tyr Asn Val Ser Ser Leu Glu Asp
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Arg Pro Ser Gln Glu Thr Ile Asn Cys Gly Asp Leu Asp Cys Arg Pro
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Pro Gly Thr Gly Gln Ser Leu Lys Pro Glu Asp His Gly Tyr Gln Cys
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615

620

Arg Met Lys Gln Leu Gln His Leu Lys Ala Gln Asn Lys His Glu Leu
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Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Ser Met Phe Ala Glu
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Lys Glu Asp Leu Phe Leu Val Asp Gln His Ala Ala Asp Glu Lys Tyr
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Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Ala Gln Arg Leu
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Ile Thr Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu Ala Val Leu
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Asp Glu Asp Ala Pro Val Thr Glu Arg Ala Lys Leu Ile Ser Leu Pro
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Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Ile Asp Glu Leu Ile
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Arg Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val Met Ile Gly
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Thr Ala Leu Asn Ala Ser Glu Met Lys Lys Leu Ile Thr His Met Gly
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Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro Thr Met Arg
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00100: 7

00110: 862

00120: FRT

00130: Homo sapiens

0400: 7

Met Glu Arg Ala Glu Ser Ser Ser Thr Glu Pro Ala Lys Ala Ile Lys
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Pro Ile Asp Arg Lys Ser Val His Gln Ile Cys Ser Gly Gln Val Val
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Leu Ser Leu Ser Thr Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp
 35 40 45

Ala Gly Ala Thr Asn Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp
 50 55 60

Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe
 65 70 75 80

Glu Gly Leu Thr Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala
 85 90 95

Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser
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Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Ala Ser
 115 120 125

Ala Lys Val Gly Thr Arg Leu Met Phe Asp His Asn Gly Lys Ile Ile
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Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Thr Thr Val Ser Val Gln
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Gln Leu Phe Ser Thr Leu Pro Val Arg His Lys Glu Phe Gln Arg Asn

165

170

175

Ile Lys Lys Glu Tyr Ala Lys Met Val Gln Val Leu His Ala Tyr Cys
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Ile Ile Ser Ala Gly Ile Arg Val Ser Cys Thr Asn Gln Leu Gly Gln
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Gly Lys Arg Gln Pro Val Val Cys Thr Gly Gly Ser Pro Ser Ile Lys
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Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile
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Pro Phe Val Gln Leu Pro Pro Ser Asp Ser Val Cys Glu Glu Tyr Gly
245 250 255

Leu Ser Cys Ser Asp Ala Leu His Asn Leu Phe Tyr Ile Ser Gly Phe
260 265 270

Ile Ser Gln Cys Thr His Gly Val Gly Arg Ser Ser Thr Asp Arg Gln
275 280 285

Phe Phe Phe Ile Asn Arg Arg Pro Cys Asp Pro Ala Lys Val Cys Arg
290 295 300

Leu Val Asn Glu Val Tyr His Met Tyr Asn Arg His Gln Tyr Pro Phe
305 310 315 320

Val Val Leu Asn Ile Ser Val Asp Ser Glu Cys Val Asp Ile Asn Val
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Thr Pro Asp Lys Arg Gln Ile Leu Leu Gln Glu Glu Lys Leu Leu Leu
340 345 350

Ala Val Leu Lys Thr Ser Leu Ile Gly Met Phe Asp Ser Asp Val Asn
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Lys Leu Asn Val Ser Gln Gln Pro Leu Leu Asp Val Glu Gly Asn Leu
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Ile Lys Met His Ala Ala Asp Leu Glu Lys Pro Met Val Glu Lys Gln
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Asp Gln Ser Pro Ser Leu Arg Thr Gly Glu Glu Lys Lys Asp Val Ser
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Ile Ser Arg Leu Arg Glu Ala Phe Ser Leu Arg His Thr Thr Glu Asn

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430

Lys Pro His Ser Pro Lys Thr Pro Glu Pro Arg Arg Ser Pro Leu Gly
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Gln Lys Arg Gly Met Leu Ser Ser Ser Thr Ser Gly Ala Ile Ser Asp
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Pro Ser Asp Pro Thr Asp Arg Ala Glu Val Glu Lys Asp Ser Gly His
 485 490 495

Gly Ser Thr Ser Val Asp Ser Glu Gly Phe Ser Ile Pro Asp Thr Gly
 500 505 510

Ser His Cys Ser Ser Glu Tyr Ala Ala Ser Ser Pro Gly Asp Arg Gly
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Ser Gln Glu His Val Asp Ser Gln Glu Lys Ala Pro Glu Thr Asp Asp
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Ser Phe Ser Asp Val Asp Cys His Ser Asn Gln Glu Asp Thr Gly Cys
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Lys Arg Phe Lys Lys Glu Glu Ile Leu Ser Ser Ser Asp Ile Cys Gln
 580 585 590

Lys Leu Val Asn Thr Gln Asp Met Ser Ala Ser Gln Val Asp Val Ala
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Val Lys Ile Asn Lys Lys Val Val Pro Leu Asp Phe Ser Met Ser Ser
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Leu Ala Lys Arg Ile Lys Gln Leu His His Glu Ala Gln Gln Ser Glu
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Gly Glu Gln Asn Tyr Arg Lys Phe Arg Ala Lys Ile Cys Pro Gly Glu
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Asn Gln Ala Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Thr Met
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Glu Lys Tyr Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Gly
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Gln Arg Leu Ile Ala Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu
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Ala Val Leu Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp
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Phe Val Ile Asp Glu Asn Ala Pro Val Thr Glu Arg Ala Lys Leu Ile
755 760 765

Ser Leu Pro Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Val Asp
770 775 780

Glu Leu Ile Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro
785 790 795 800

Ser Arg Val Lys Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val
805 810 815

Met Ile Gly Thr Ala Leu Asn Thr Ser Glu Met Lys Lys Leu Ile Thr
820 825 830

His Met Gly Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro
835 840 845

Thr Met Arg His Ile Ala Asn Leu Gly Val Ile Ser Gln Asn
850 855 860

00100 -

00110 - 2771

0012 - DNA

0013 - Homo sapiens

0400 -

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(112): PFT

(113): Homo sapiens

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275 280 285

Thr Arg Leu Tyr Pro Val Phe Phe Leu Lys Ile Asp Val Pro Thr Ala
290 295 300

Asp Val Asp Val Asn Leu Thr Pro Asp Lys Ser Gln Val Leu Leu Gln
305 310 315 320

Asn Lys Glu Ser Val Leu Ile Ala Leu Glu Asn Leu Met Thr Thr Cys
325 330 335

Tyr Gly Pro Leu Pro Ser Thr Asn Ser Tyr Glu Asn Asn Lys Thr Asp
340 345 350

Val Ser Ala Ala Asp Ile Val Leu Ser Lys Thr Ala Glu Thr Asp Val
355 360 365

Leu Phe Asn Lys Val Glu Ser Ser Gly Lys Asn Tyr Ser Asn Val Asp
370 375 380

Thr Ser Val Ile Pro Phe Gln Asn Asp Met His Asn Asp Glu Ser Gly
385 390 395 400

Lys Asn Thr Asp Asp Cys Leu Asn His Gln Ile Ser Ile Gly Asp Phe
405 410 415

Gly Tyr Gly His Cys Ser Ser Glu Ile Ser Asn Ile Asp Lys Asn Thr
420 425 430

Lys Asn Ala Phe Gln Asp Ile Ser Met Ser Asn Val Ser Trp Glu Asn
435 440 445

Ser Gln Thr Glu Tyr Ser Lys Thr Cys Phe Ile Ser Ser Val Lys His
450 455 460

Thr Gln Ser Glu Asn Gly Asn Lys Asp His Ile Asp Glu Ser Gly Glu
465 470 475 480

Asn Glu Glu Glu Ala Gly Leu Glu Asn Ser Ser Glu Ile Ser Ala Asp
485 490 495

Glu Trp Ser Arg Gly Asn Ile Leu Lys Asn Ser Val Gly Glu Asn Ile
500 505 510

Glu	Pro	Val	Lys	Ile	Leu	Val	Pro	Glu	Lys	Ser	Leu	Pro	Cys	Lys	Val	515	520	525
Ser	Asn	Asn	Asn	Tyr	Pro	Ile	Pro	Glu	Gln	Met	Asn	Leu	Asn	Glu	Asp	530	535	540
Ser	Cys	Asn	Lys	Lys	Ser	Asn	Val	Ile	Asp	Asn	Lys	Ser	Gly	Lys	Val	545	550	555
Thr	Ala	Tyr	Asp	Leu	Leu	Ser	Asn	Arg	Val	Ile	Lys	Lys	Pro	Met	Ser	565	570	575
Ala	Ser	Ala	Leu	Phe	Val	Gln	Asp	His	Arg	Pro	Gln	Phe	Leu	Ile	Glu	580	585	590
Asn	Pro	Lys	Thr	Ser	Leu	Glu	Asp	Ala	Thr	Leu	Gln	Ile	Glu	Glu	Leu	595	600	605
Trp	Lys	Thr	Leu	Ser	Glu	Glu	Glu	Lys	Leu	Lys	Tyr	Glu	Glu	Lys	Ala	610	615	620
Thr	Lys	Asp	Leu	Glu	Arg	Tyr	Asn	Ser	Gln	Met	Lys	Arg	Ala	Ile	Glu	625	630	635
Gln	Glu	Ser	Gln	Met	Ser	Leu	Lys	Asp	Gly	Arg	Lys	Lys	Ile	Lys	Pro	645	650	655
Thr	Ser	Ala	Trp	Asn	Leu	Ala	Gln	Lys	His	Lys	Leu	Lys	Thr	Ser	Leu	660	665	670
Ser	Asn	Gln	Pro	Lys	Leu	Asp	Glu	Leu	Leu	Gln	Ser	Gln	Ile	Glu	Lys	675	680	685
Arg	Arg	Ser	Gln	Asn	Ile	Lys	Met	Val	Gln	Ile	Pro	Phe	Ser	Met	Lys	690	695	700
Asn	Leu	Lys	Ile	Asn	Phe	Lys	Lys	Gln	Asn	Lys	Val	Asp	Leu	Glu	Glu	705	710	715
Lys	Asp	Glu	Pro	Cys	Leu	Ile	His	Asn	Leu	Arg	Phe	Pro	Asp	Ala	Trp	725	730	735
Leu	Met	Thr	Ser	Lys	Thr	Glu	Val	Met	Leu	Leu	Asn	Pro	Tyr	Arg	Val	740	745	750
Glu	Glu	Ala	Leu	Leu	Phe	Lys	Arg	Leu	Leu	Glu	Asn	His	Lys	Leu	Pro	755	760	765

Ala Glu Pro Leu Glu Lys Pro Ile Met Leu Thr Glu Ser Leu Phe Asn
770 775 780

Gly Ser His Tyr Leu Asp Val Leu Tyr Lys Met Thr Ala Asp Asp Gln
785 790 795 800

Arg Tyr Ser Gly Ser Thr Tyr Leu Ser Asp Pro Arg Leu Thr Ala Asn
805 810 815

Gly Phe Lys Ile Lys Leu Ile Pro Gly Val Ser Ile Thr Glu Asn Tyr
820 825 830

Leu Glu Ile Glu Gly Met Ala Asn Cys Leu Pro Phe Tyr Gly Val Ala
835 840 845

Asp Leu Lys Glu Ile Leu Asn Ala Ile Leu Asn Arg Asn Ala Lys Glu
850 855 860

Val Tyr Glu Cys Arg Pro Arg Lys Val Ile Ser Tyr Leu Glu Gly Glu
865 870 875 880

Ala Val Arg Leu Ser Arg Gln Leu Pro Met Tyr Leu Ser Lys Glu Asp
885 890 895

Ile Gln Asp Ile Ile Tyr Arg Met Lys His Gln Phe Gly Asn Glu Ile
900 905 910

Lys Glu Cys Val His Gly Arg Pro Phe Phe His His Leu Thr Tyr Leu
915 920 925

Pro Glu Thr Thr
930

4210 + 10

4211 + 3063

4212 + DNA

4213 + Homo sapiens

4400 + 10

ggcagcagtg gctgcttgcg gctagtgcat ggtaattgcc tgcctgcgcg tagcagcag 60
ctgctctggtt aaaagcgaaa atgaaacaat tgcctgcgcg aacagttcga ctctttcaca 120
gttctcagat catcacttcg gtggtcagtg ttgtaaaaga gcttattgaa aactcttgg 180
atgttggtgc cacaagcgta gatgttaaac tggagaacta tggatttgat aaaattgagg 240
tgcgagataa cggggagggt atcaaggctg ttgatgcacc tgtaattgca atgaagtaac 300
acacotcaaa aataaatagt catgaagatc ttgaaaattt gacaacttac ggttttcgtg 360
gagaagcctt ggggtcaatt tgttgtatag ctgaggtttt aattacaaca agaaogcgctg 420

ctgataat	tttagcaccag	tatgttttag	atggcagtg	ccacataatt	tctcagaaaa	480
cttcacatct	tggtaaggt	acaaactgtaa	ctgctttaag	attatttaag	aatctacotg	540
taagaaagca	gttttaactca	actgcaaaaa	aatgttaaaga	tgaaataaaa	aagatccaaag	600
atctctctcat	gagctttggg	atccttaaac	ctgaacttaag	gatttgtctt	gtacataaca	660
aggcagttat	ttggcagaaa	agcagagtat	cagatccaaa	gatggctctc	atctcagttc	720
tggggaactgc	tggttatgaac	aatatggaat	cttttcagta	ccactctgaa	gaktctcaga	780
tttatctcag	tggatttctt	ccaaagtgtg	atgcagacca	ctctttcaat	agttcttcaa	840
caccagaaaag	aagtttcctc	ttcataaaca	gtcgaccagt	acatcaaaaa	gatatcttaa	900
agttaatccg	acatcattac	aatctgaaat	gcttaaaagga	atctactctg	ttgtatctctg	960
ttctctctct	gaaaatcctat	gttctctcag	ctgatgttga	tgtaaattta	acaccagata	1020
aaagccaagt	attattacaa	aataaggaat	ctgttttaat	tgtctctgaa	aatctgatga	1080
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ccgcagctga	catcgttctt	agtaaaacag	cagaaacaga	tgtgctttt	aaaaaagtg	1200
aatcctctgg	aaagaattat	tcaaatgtt	atacttcagt	cattccattc	caaaatgata	1260
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gtgactttgg	ttatggctcat	tgtagtagtg	aaattttctaa	cattgataaa	aacactaaga	1380
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ctgcagatga	gtggagccagg	gaaaatatac	ttaaaaattc	agtgggagag	aatattgaac	1620
ctgtgaaaat	tttagtgctt	gaaaaaagtt	taccatgtta	agtaagtta	aatattcttc	1680
caatccctga	acaaatgaat	cttaatgaag	attcatgtta	caaaaaatca	aagttaatat	1740
ataataaata	tggaaaagtt	acagcttatg	atttactttg	caatcgagta	atcaagaaac	1800
ccatgttcagc	aagtgtctct	tttgttcaag	atcatctctc	tcagtttctc	atagaaaata	1860
ctaagactag	tttagaggat	gcaacattac	aaattgaaga	actgtgggaa	acattgagtg	1920
aagaggaaaa	actgaaatat	gaagagaagg	ctacttaaga	cttggaacga	tacaatatgc	1980
aatgaagag	agccattgaa	caggagtcac	aaatgtcact	aaaagatggc	agaaaaaaga	2040
taaaaaccac	cagcgcattg	aatttcggccc	agaagcacaa	gttaaaaaac	tcattatcta	2100
atcaaccaaa	acttgatgaa	ctccttcagt	cccaaatgta	aaaaagaagg	agtcaaaaata	2160
ttaaaaatggt	acagatcccc	ttttctatga	aaaaactaaa	aataaatttt	aagaaaacaaa	2220
acaaaagctga	cttagaagag	aaggatgaac	cttgcttgat	ccacaatctc	aggtttctctg	2280
atgcctgggt	aatgacatcc	aaaacagagg	taatgttatt	aaatccatat	agagtagaag	2340
aagccctgtt	atttaaaaaga	cttcttgaga	atcataaaat	tcctgcagag	ccactggaaa	2400
agccaattat	gttaacagag	agtcttttta	atggacttca	ttatttagac	gttttatata	2460
aaatgacagc	agatgaccaa	agatacagtg	gatcaactta	ctgtctgat	ctcctgtotta	2520
cagcgaatgg	tttcaagata	aaattgatac	caggagtttc	aattactgaa	aattacttgg	2580
aaatagaagg	aatggctaat	tgtctcccat	tctatggagt	agcagattta	aaagaaattc	2640
ttaatgttat	attaaacaga	aatgcaaaag	aagtttatga	atgtagacct	cgcbaagtga	2700
taagttat	agaggagaa	gcagtgcctc	tatccagaca	attacccatg	tacttatcaa	2760
aagaggacat	ccaagacatt	atctacagaa	tgaagcacca	gtttggaaat	gaaattaaag	2820
agtgtgttca	tggctgcaca	ttttttcctc	atttaacctc	tcttcagaa	actacatgat	2880
taaaatgtt	taagaagatt	agttaccatt	gaaattgggt	ctgtcataaa	acagcatgag	2940
tctgttttta	aattatcttt	gtattatgtg	tcacatgggt	attttttaaa	tgaggattca	3000
ctgacttggt	tttatattga	aaaaagttcc	acgtattgta	gaaaacgtaa	ataaactaat	3060
aac						3120

02110 934

02120 PRT

02130 Homo sapiens

04000 11

Met Ala Val Gln Pro Lys Glu Thr Leu Gln Leu Glu Ser Ala Ala Glu
1 5 10 15

Val Gly Phe Val Arg Phe Phe Gln Gly Met Pro Glu Lys Pro Thr Thr
20 25 30

Thr Val Arg Leu Phe Asp Arg Gly Asp Phe Tyr Thr Ala His Gly Glu
35 40 45

Asp Ala Leu Leu Ala Ala Arg Glu Val Phe Lys Thr Gln Gly Val Ile
50 55 60

Lys Tyr Met Gly Pro Ala Gly Ala Lys Asn Leu Gln Ser Val Val Leu
65 70 75 80

Ser Lys Met Asn Phe Glu Ser Phe Val Lys Asp Leu Leu Leu Val Arg
85 90 95

Gln Tyr Arg Val Glu Val Tyr Lys Asn Arg Ala Gly Asn Lys Ala Ser
100 105 110

Lys Glu Asn Asp Trp Tyr Leu Ala Tyr Lys Ala Ser Pro Gly Asn Leu
115 120 125

Ser Gln Phe Glu Asp Ile Leu Phe Gly Asn Asn Asp Met Ser Ala Ser
130 135 140

Ile Gly Val Val Gly Val Lys Met Ser Ala Val Asp Gly Gln Arg Gln
145 150 155 160

Val Gly Val Gly Tyr Val Asp Ser Ile Gln Arg Lys Leu Gly Leu Cys
165 170 175

Glu Phe Pro Asp Asn Asp Gln Phe Ser Asn Leu Glu Ala Leu Leu Ile
180 185 190

Gln Ile Gly Pro Lys Glu Cys Val Leu Pro Gly Gly Glu Thr Ala Gly
195 200 205

Asp Met Gly Lys Leu Arg Gln Ile Ile Gln Arg Gly Gly Ile Leu Ile
210 215 220

Thr Glu Arg Lys Lys Ala Asp Phe Ser Thr Lys Asp Ile Tyr Gln Asp

225

230

235

240

Leu Asn Arg Leu Leu Lys Gly Lys Lys Gly Glu Gln Met Asn Ser Ala
245 250 255

Val Leu Pro Glu Met Glu Asn Gln Val Ala Val Ser Ser Leu Ser Ala
260 265 270

Val Ile Lys Phe Leu Glu Leu Leu Ser Asp Asp Ser Asn Phe Gly Gln
275 280 285

Phe Glu Leu Thr Thr Phe Asp Phe Ser Gln Tyr Met Lys Leu Asp Ile
290 295 300

Ala Ala Val Arg Ala Leu Asn Leu Phe Gln Gly Ser Val Glu Asp Thr
305 310 315 320

Thr Gly Ser Gln Ser Leu Ala Ala Leu Leu Asn Lys Cys Lys Thr Pro
325 330 335

Gln Gly Gln Arg Leu Val Asn Gln Trp Ile Lys Gln Pro Leu Met Asp
340 345 350

Lys Asn Arg Ile Glu Glu Arg Leu Asn Leu Val Glu Ala Phe Val Glu
355 360 365

Asp Ala Glu Leu Arg Gln Thr Leu Gln Glu Asp Leu Leu Arg Arg Phe
370 375 380

Pro Asp Leu Asn Arg Leu Ala Lys Lys Phe Gln Arg Gln Ala Ala Asn
385 390 395 400

Leu Gln Asp Cys Tyr Arg Leu Tyr Gln Gly Ile Asn Gln Leu Pro Asn
405 410 415

Val Ile Gln Ala Leu Glu Lys His Glu Gly Lys His Gln Lys Leu Leu
420 425 430

Leu Ala Val Phe Val Thr Pro Leu Thr Asp Leu Arg Ser Asp Phe Ser
435 440 445

Lys Phe Gln Glu Met Ile Glu Thr Thr Leu Asp Met Asp Gln Val Glu
450 455 460

Asn His Glu Phe Leu Val Lys Pro Ser Phe Asp Pro Asn Leu Ser Glu
465 470 475 480

Leu Arg Glu Ile Met Asn Asp Leu Glu Lys Lys Met Gln Ser Thr Leu

Ile Ser Ala Ala Arg Asp Leu Gly Leu Asp Pro Gly Lys Gln Ile Lys
500 505 510

Leu Asp Ser Ser Ala Gln Phe Gly Tyr Tyr Phe Arg Val Thr Cys Lys
515 520 525

Glu Glu Lys Val Leu Arg Asn Asn Lys Asn Phe Ser Thr Val Asp Ile
530 535 540

Gln Lys Asn Gly Val Lys Phe Thr Asn Ser Lys Leu Thr Ser Leu Asn
545 550 555 560

Glu Glu Tyr Thr Lys Asn Lys Thr Glu Tyr Glu Glu Ala Gln Asp Ala
565 570 575

Ile Val Lys Glu Ile Val Asn Ile Ser Ser Gly Tyr Val Glu Pro Met
580 585 590

Gln Thr Leu Asn Asp Val Leu Ala Gln Leu Asp Ala Val Val Ser Phe
595 600 605

Ala His Val Ser Asn Gly Ala Pro Val Pro Tyr Val Arg Pro Ala Ile
610 615 620

Leu Glu Lys Gly Gln Gly Arg Ile Ile Leu Lys Ala Ser Arg His Ala
625 630 635 640

Cys Val Glu Val Gln Asp Glu Ile Ala Phe Ile Pro Asn Asp Val Tyr
645 650 655

Phe Glu Lys Asp Lys Gln Met Phe His Ile Ile Thr Gly Pro Asn Met
660 665 670

Gly Gly Lys Ser Thr Tyr Ile Arg Gln Thr Gly Val Ile Val Leu Met
675 680 685

Ala Gln Ile Gly Cys Phe Val Pro Cys Glu Ser Ala Glu Val Ser Ile
690 695 700

Val Asp Cys Ile Leu Ala Arg Val Gly Ala Gly Asp Ser Gln Leu Lys
705 710 715 720

Gly Val Ser Thr Phe Met Ala Glu Met Leu Gln Thr Ala Ser Ile Leu
725 730 735

Arg Ser Ala Thr Lys Asp Ser Leu Ile Ile Ile Asp Glu Leu Gly Arg

740

745

750

Gly Thr Ser Thr Tyr Asp Gly Phe Gly Leu Ala Trp Ala Ile Ser Glu
755 760 765

Tyr Ile Ala Thr Lys Ile Gly Ala Phe Cys Met Phe Ala Thr His Phe
770 775 780

His Glu Leu Thr Ala Leu Ala Asn Gln Ile Pro Thr Val Asn Asn Leu
785 790 795 800

His Val Thr Ala Leu Thr Thr Glu Glu Thr Leu Thr Met Leu Tyr Gln
805 810 815

Val Lys Lys Gly Val Cys Asp Gln Ser Phe Gly Ile His Val Ala Glu
820 825 830

Leu Ala Asn Phe Pro Lys His Val Ile Glu Cys Ala Lys Gln Lys Ala
835 840 845

Leu Glu Leu Glu Glu Phe Gln Tyr Ile Gly Glu Ser Gln Gly Tyr Asp
850 855 860

Ile Met Glu Pro Ala Ala Lys Lys Cys Tyr Leu Glu Arg Glu Gln Gly
865 870 875 880

Glu Lys Ile Ile Gln Glu Phe Leu Ser Lys Val Lys Gln Met Pro Phe
885 890 895

Thr Glu Met Ser Glu Glu Asn Ile Thr Ile Lys Leu Lys Gln Leu Lys
900 905 910

Ala Glu Val Ile Ala Lys Asn Asn Ser Phe Val Asn Glu Ile Ile Ser
915 920 925

Arg Ile Lys Val Thr Thr
930

00100 12

00110 3145

00120 DNA

00130 Homo sapiens

00000 12

ggcgggaaac agcttagtgg gtgtgggggtc ggcgattttc ttcaaccagg aggtgaggag 60
gtttcgacat ggcgggtgcag ccgaaggaga cgtgcagtt ggagagcgcg gcgaggtcg 120
gtttgtgog cttcttttcag ggcattgcgg agaagccgac caccacagtg cgccttttcg 180

acccgggggga	ottotataag	gggaacggg	aggacggggt	gotggggggg	ggggagggtgt	210
tcaagacccca	gggggtgato	aagtaacatgg	ggcgggacagg	agcaaaagaat	ctgcagaggtg	311
ttgtgotttag	taaaatgaat	tttgaatott	ttgtaaaaga	tottotttttg	gttcgttcagt	310
atagagttga	agtttataag	aatagaggtg	gaaataaggg	atccaaaggag	aatgatttgg	410
atttggcata	taaggotttt	ccgggcaatc	tctctcagtt	tgaagacatt	ctcttttggt	410
acaatgatat	gtcagotttc	attgggtgtg	tgggtgttaa	aatgtccggc	gttgatgggc	510
agagacaggt	tggagttggg	tatgtggatt	ccatacagag	gaaaactagga	ctgtgtgaat	611
tccctgataa	tgatcagttc	tccaattttg	aggetctctc	catacagatt	ggaccaagg	610
aatgtgtttt	acccggagga	gagactgtgt	gagacatggg	gaaaactgaga	cagataattc	710
aaagaggagg	aattctgato	acagaaagaa	aaaaagctga	cttttccaca	aaagacattt	711
atcaggacct	caacgggttg	ttgaaaagca	aaaaggggaga	gcagatgaat	agtgtgtgat	811
tgcacagaaat	ggagaatcag	gttgcaagttt	catactgttc	tgcggttaac	aagttttttag	911
aactcttata	agatgatttc	aacttttgac	agttttgaact	gactactctt	gaatttcagc	910
actatatgaa	attggatatt	gcagcactca	gagcccttaa	cttttttcag	gggtctgttg	1010
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gacaaagact	gtttaaccag	tggatttaag	agctctctct	ggataagaac	agaatagagg	111
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cagcaaacct	acaagattgt	tacgcactct	atcagggtat	aatcaacta	actaatgtta	1311
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gtgcagccag	agatcttggc	tgtjaactgt	gcnaacagat	ttaaactgja	tcagtgcaac	1611
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cttttaaata	agagtataac	aaaaataaaa	cagaatatja	agaagccacg	gatgcacattg	1800
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tgttagctca	gctagatgct	gttgtcagct	ttgtctacgt	gtcaaatgga	gcacctgttc	1920
catatgtacg	accagccatt	tggagagaa	gacaagggaag	aattatatta	aaagcatcca	1960
ggcatgcttg	tgttgaaagt	caagatgaaa	ttgcatttat	tcctaattgac	gtataactttg	2040
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gagaatcgca	aggatatgat	atcatggaac	cagcagcaaa	gaagtgttat	ctggaaaagag	2700
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cagtaatgga	atgaaggtaa	tattgataag	ctattgtctg	taatatgttt	atattgtttt	2940
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. gctgtaactg aggactgttt gcaattgaca taggcaataa taagtgaatgt gctgaatttt 3120
 ataaataaaa tcatgtagtt tgtgg 3145

4210: 13
 4211: 756
 4212: PRT
 4213: Homo sapiens

4400: 13
 Met Ser Phe Val Ala Gly Val Ile Arg Arg Leu Asp Glu Thr Val Val
 1 5 10 15

Asn Arg Ile Ala Ala Gly Glu Val Ile Gln Arg Pro Ala Asn Ala Ile
 20 25 30

Lys Glu Met Ile Glu Asn Cys Leu Asp Ala Lys Ser Thr Ser Ile Gln
 35 40 45

Val Ile Val Lys Glu Gly Gly Leu Lys Leu Ile Gln Ile Gln Asp Asn
 50 55 60

Gly Thr Gly Ile Arg Lys Glu Asp Leu Asp Ile Val Cys Glu Arg Phe
 65 70 75 80

Thr Thr Ser Lys Leu Gln Ser Phe Glu Asp Leu Ala Ser Ile Ser Thr
 85 90 95

Tyr Gly Phe Arg Gly Glu Ala Leu Ala Ser Ile Ser His Val Ala His
 100 105 110

Val Thr Ile Thr Thr Lys Thr Ala Asp Gly Lys Cys Ala Tyr Arg Ala
 115 120 125

Ser Tyr Ser Asp Gly Lys Leu Lys Ala Pro Pro Lys Pro Cys Ala Gly
 130 135 140

Asn Gln Gly Thr Gln Ile Thr Val Glu Asp Leu Phe Tyr Asn Ile Ala
 145 150 155 160

Thr Arg Arg Lys Ala Leu Lys Asn Pro Ser Glu Glu Tyr Gly Lys Ile
 165 170 175

Leu Glu Val Val Gly Arg Tyr Ser Val His Asn Ala Gly Ile Ser Phe
 180 185 190

Ser Val Lys Lys Gln Gly Glu Thr Val Ala Asp Val Arg Thr Leu Pro
 195 200 205

Asn Ala Ser Thr Val Asp Asn Ile Arg Ser Ile Phe Gly Asn Ala Val
210 215 220

Ser Arg Glu Leu Ile Glu Ile Gly Cys Glu Asp Lys Thr Leu Ala Phe
225 230 235 240

Lys Met Asn Gly Tyr Ile Ser Asn Ala Asn Tyr Ser Val Lys Lys Cys
245 250 255

Ile Phe Leu Leu Phe Ile Asn His Arg Leu Val Glu Ser Thr Ser Leu
260 265 270

Arg Lys Ala Ile Glu Thr Val Tyr Ala Ala Tyr Leu Pro Lys Asn Thr
275 280 285

His Pro Phe Leu Tyr Leu Ser Leu Glu Ile Ser Pro Gln Asn Val Asp
290 295 300

Val Asn Val His Pro Thr Lys His Glu Val His Phe Leu His Glu Glu
305 310 315 320

Ser Ile Leu Glu Arg Val Gln Gln His Ile Glu Ser Lys Leu Leu Gly
325 330 335

Ser Asn Ser Ser Arg Met Tyr Phe Thr Gln Thr Leu Leu Pro Gly Leu
340 345 350

Ala Gly Pro Ser Gly Glu Met Val Lys Ser Thr Thr Ser Leu Thr Ser
355 360 365

Ser Ser Thr Ser Gly Ser Ser Asp Lys Val Tyr Ala His Gln Met Val
370 375 380

Arg Thr Asp Ser Arg Glu Gln Lys Leu Asp Ala Phe Leu Gln Pro Leu
385 390 395 400

Ser Lys Pro Leu Ser Ser Gln Pro Gln Ala Ile Val Thr Glu Asp Lys
405 410 415

Thr Asp Ile Ser Ser Gly Arg Ala Arg Gln Gln Asp Glu Glu Met Leu
420 425 430

Glu Leu Pro Ala Pro Ala Glu Val Ala Ala Lys Asn Gln Ser Leu Glu
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Ile Asn Glu Gln Gly His Glu Val Leu Arg Glu Met Leu His Asn His
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Ser Phe Val Gly Cys Val Asn Pro Gln Trp Ala Leu Ala Gln His Gln
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Tyr Phe Ser Leu Glu Ile Asp Glu Glu Gly Asn Leu Ile Gly Leu Pro
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Phe Glu Ser Leu Ser Lys Glu Cys Ala Met Phe Tyr Ser Ile Arg Lys
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Tyr Lys Ala Leu Arg Ser His Ile Leu Pro Pro Lys His Phe Thr Glu
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